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# Formulation and Evaluation of Lamotrigine 25 Mg Immediate Release Tablet

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## ABSTRACT

In the present quality assurance research work Lamotrigine Immediate Release tablet25mg has been undertaken in accordance with Quality By Design guidelines. Quality by design a common understanding of the concept of ICH guideline Q8, Q9 & Q10 is now a day treaded as an essential tool in the process of formulation development. The development of Target Product Profile & Critical Quality Attributes were done after dew consideration of risk assessment before finalization of these attributes. As Lamotrigine is poorly soluble (BCS class-II) it may effect bioavailability, Hence, Solid dispersion approach was taken as risk assessment measure. Product design space & process parameters were finalized on the basis of critical material attributes. Control strategies for continuous monitoring & updating of the process requirements were also highlighted. In the present research work critical process parameters were validated. The critical process parameter impacts on Quality. The Quality By Design principle & tools demonstrated in present research work will be useful in creating & developing control strategies in similar formulation & process development.

**Keywords:** QbD, Solid dispersion, ICH Guidelines.

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## INTRODUCTION

The term convulsion refers to a transient alteration of behavior due to the disordered, synchronous & rhythmic firing of pupations of brain neurons. The term epilepsy refers to a disorder of brain function characterized by the periodic & unpredictable occurrence of seizures.

The convulsions are common & frequently devastating disorders, affecting approximately 2.5 million people in the United States alone. Epileptic seizures often caused by transient impairment of consciousness, leaving the individual at risk of bodily harm and often interfering with education & employment. Lamotrigine is a phenyltriazine derivative initially developed as an antifolate agent based upon the incorrect idea that reducing folate would effectively combact seizures. Structure activity studies indicate that its effectiveness as an anti seizure drug is unrelated to its antifolate properties. It was approved by the food & drug administration in 1994. [1] The general principle of drug therapy of the epilepsies are summarize below, lamotrigine is a anticonvulsant agent. Lamotrigine suppresses tonic hindlimb &partial & secondarily generalized seizures. Lamotrigine blocks sustained repetitive firing of mouse spinal cord neurons & delays the recovery from inactivation of recombinant $Na^+$ channels. This may well explain lamotrigines action on partial & secondarily generalized seizures. Lamotrigine is effective against a broader spectrum of seizures, suggesting that lamotrigine may have actions in addition to regulating recovery from inactivation of $Na^+$ channels. Patients who already taking a hepatic enzyme – including antiseizure drugs should be given lamotrigine initially at 50 mg per day for 2 weeks. The dose is increased to 50 mg twice per day for 2 weeks & then increased in increments of 100 mg/day each week up to a maintenance dose of 300 to 500mg/day divided into two doses.

## MATERIAL AND METHODS

**Table 1: List of Materials Used**

| S. N. | Name of Materials | Supplied By/Gifted By |
|---|---|---|
| 1 | Lamotrigine | RA Chem Pharma Ltd (Hyd) as a gift sample |
| 2 | Polyetrhylene glycol | Research Lab Fine Chem Industry, Mumbai. |
| 3 | Lactose | Pallav chemical & solvent PVT. LTD. |
| 4 | Magnesium stearate | Highlab chemicals |
| 5 | Sodium starch glycolate | Research Lab Fine Chem Industry, Mumbai. |
| 6 | Talc | Thermosil Fine Chem Industry |
| 7 | Acetone | Research Lab Fine Chem Industry, Mumbai. |

**Compression**[2]

Step 1- weighed required quantity of soli dispersion & pass through 40 mesh sieve.

Step2-weight lactose pass through 40 mesh sieve.& put in to V blender. Check mesh size & intact mesh.

Step3- Add lactose, sodium starch glycolate, talc, magnesium stearate & solid dispersion in ascending order of blending.

Step 4- Compress the tablet using a tablet compression machine.

**Table 2: Tablet Formula**

| S. N. | Ingredient name | Analytical report | Quantity per tablet | For 1000 tablet |
|---|---|---|---|---|
| 1 | Solid dispersion equivalent to API | 0.001 | 50mg | 50gm |
| 2 | Lactose | 0.002 | 73mg | 73gm |
| 3 | Talc | 0.003 | 15mg | 15gm |
| 4 | Sodium starch glycolate | 0.004 | 7.5mg | 7.5gm |
| 5 | Magnesium stearate | 0.005 | 4.5mg | 4.5gm |

**Evaluation and Result** [3,4]

**Hardness**:

Tablet hardness is also known as tablet crushing strength & was determined by Monsanto hardness tester. It applies force to the tablet diametrically with the help of an in built spring. TrIP 2014()licate determinations were done. The hardness of the tablet is measured by using conventional hardness testers like Monsanto hardness tester.

**Thickness**:

The crown thickness of individual tablet from all the formulation was measured using screw gauge.

**Friability**:

Friability test is performed to assess the effect of abrasions and shock that may often cause tablet to chip, cap or break. Roche Friabilator was used for the purpose. For tablets with a unit weight equal to or less than 650 mg, take a sample of whole tablets corresponding as near as possible to 6.5 g. For tablets with a unit weight of more than 650 mg, take a sample of 10 whole tablets. The tablets should be carefully dedusted prior to testing. Accurately weigh the tablet sample, and place the tablets in the drum. Rotate the drum 100 times, and remove the tablets. Remove any loose dust from the tablets as before, and accurately weigh.

**% F= (Wo – W / Wo) ×100**

Where, **% F**= Friability in percentage

**Wo**= Initial weight of tablet

**W**= Final weight after revolution.

**Weight variation**:

Weigh individually 20 whole tablets, and calculate the average weight. The requirements are met if the weights of not more than 2 of the tablets differ from the average weight by more than the percentage listed in the accompanying table and no tablet differs in weight by more than double that percentage

**Drug content uniformity**:

The Lamotrigine content in tablets was determined by powdering 10 tablets in each batch. Powder equivalent to 100 mg of Lamotrigine was dissolved in 0.1 N HCl. 1 ml of filtrate was further diluted to 100 ml with 0.1 N HCl and it was determined by spectroscopy at 340 nm.

**Disintegration time:**

The disintegration test was performed using Electrolab disintegrating apparatus. Six tablets were selected randomly from each batch for the disintegration test.Placed one tablet in each of the six tubes of the basketand operate the Disintegration apparatus using in simulated gastric fluid maintained at 37±0.5ºC. Disintegration time (DT) was measured for immediate release layer.

Table No 3: Post Compression Study

| Hardness ($kg/cm^2$) | Thickness | Friability % | Weight variation (mg) | Drug content (%) | Disintegration time (second) |
|---|---|---|---|---|---|
| 3.7 | 1.7 | 0.41 | 150.03 | 97.75 | 134 |

**Dissolution study:**

In-vitro dissolution studies of floating tablets were carried out in USP dissolution test apparatus-II, employing a paddle type apparatus at 50 rpm using 900ml of 0.1N HCl as dissolution medium at 37±0.5ºC. One tablet was used in each test. At predetermined time intervals 5ml of the samples were withdrawn by means of a syringe. The volume withdrawn at each interval was replaced with same quantity of fresh dissolution medium maintained at 37±0.5ºC. The withdrawn samples were filtered through membrane filter 0.45µm & analyzed by using UV spectrophotometer at λ max 240 nm. This test was performed on 9 batches of immediate release tablets.

Medium : - 0.1N HCl
Temperature : - 37 ± 0.5ºC
Volume : - 900 ml.
RPM : - 50
Apparatus : - Dissolution apparatus USP type II.
Time :- 30 mins

**Calibration Curve of Lamotrigine-**

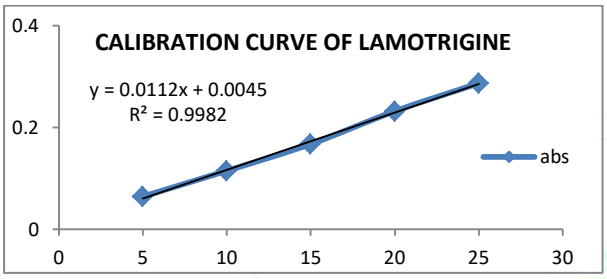


Fig No.1 : Calibration Curve Of Lamotrigine

**Percentage Drug Release:**

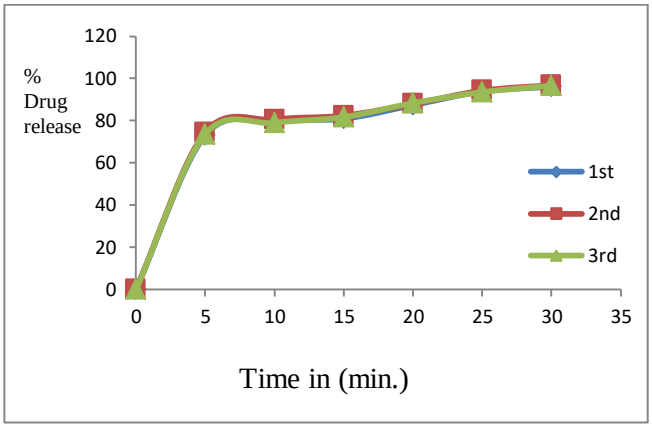


Fig. No. 2 : Percentage drug release for Lamotrigine immediate release tablet

**Stability Testing [5]**

For long term studies, frequency of testing should be sufficient to establish the stability profile of the drug substance. At the accelerated storage condition, a minimum of three time points, including the initial and final time point (e. g 0, 3 and 6 months), from a 6- month study was recommended. When testing at the intermediate storage condition is called for as a result of significant change at the accelerated storage.

Table 4: Result of Stability Testing

| Parameters | Initial | After 1 month | After 2 month | After 3 month |
|---|---|---|---|---|
| | Temp :40⁰ c±2⁰ c Humidity :75 ± 5% RH | Temp :40⁰ c±2⁰ c Humidity :75 ± 5% RH | | |
| **Hardness(3 to 5 kg/cm²)** | 3.7 | 3.72 | 3.75 | 3.78 |
| **Disintegration time(sec)NMT 3 min** | 134 | 134 | 135 | 138 |
| **Drug content (90 to 101%)** | 95.75 | 95.75 | 94.87 | 94.23 |
| **Appearance** | White tablet | White tablet | White tablet | White tablet |

The product meets the stability requirement for 6 month as per ICH guideline.

## CONCLUSION

The present research work highlighted all the activities involved to built quality into the product using quality by design techniques research work. All the steps such as identification of target product profile , critical quality attributes, product design space, process design space, risk assessment & product characterization were conducted systematically. Additionally critical quality attributes& control strategy & process validation were also carried out. The stability data shows the product is stable at 40⁰c ± 2⁰c for 3 months at 75 ± 5% RH . The experimentation were planed as per plan of work & all the recommended parameters of quality by design requirement as per ICH Q2 (R1) guidelines were followed step wise. This research work highlights that there are many strategic control points which are required to be addressed systematically to achieve quality assurance requirements in the manufacturing & control of pharmaceutical formulations to ensure that the quality is built in to the product.

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